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TITLE: Changes in Ovarian Stromal Function in Premenopausal Women Undergoing Chemotherapy for Breast Cancer

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13. Abstract (Maximum 200 Words) (abstract should contain no proprietary or confidential information) The purpose of this clinical research training grant is to gain the expertise to develop a program of research regarding understudied, critical quality of life issues in breast cancer survivors. A pilot research project was developed to look at the effect of chemotherapy on ovarian stromal function in premenopausal women undergoing chemotherapy for breast cancer. In this pilot study to assess ovarian stromal function, androgen levels will be drawn and evaluated at baseline and over the course of chemotherapy as the ovarian stroma is a significant source of androgens in naturally postmenopausal women. As androgens are linked in the literature to several symptoms that women with breast cancer experience, specifically decreased libido, increased fatigue, negative mood, vasomotor symptoms, and weight gain, it is important to explore the potential role of androgens in the etiologies of these symptoms. Nothing is known about this area currently in breast cancer survivors. Through the process of writing the pilot study and attending educational sessions, this principal investigator has continued to develop expertise in the area of sexuality and endocrine function as they relate to breast cancer survivors. A published review article on libido and a presentation on endocrine changes in breast cancer survivors have resulted.				
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Introduction:

This grant is a clinical research nurse training grant that has two components. The first is to develop, implement, analyze and publish a pilot study that will provide data for a more definitive extramurally funded study. The second is for the principal investigator to be mentored and educated toward being an independent clinical nurse researcher.

Body:

The approved statement of work includes seven tasks over the 24 month period.

Task 1: Work with the collaborative team to develop the working protocol of the pilot study, "Changes in ovarian stromal function in premenopausal women receiving chemotherapy for breast cancer". *Task 1 has been completed in that the team has been assembled and the active protocol has been written. The team includes an endocrinologist, statistician, my mentor, as well as breast cancer clinicians.*

Task 2: Ongoing mentoring and educational sessions throughout the two years. *With respect to the mentoring and educational meetings, task 2 is ongoing with weekly meetings with mentor (Dr. Loprinzi), twice monthly budget administration meetings, monthly cancer control/symptom management meetings and breast committee meetings. In addition, team meetings in symptom management have occurred providing experience for this trainee to work in leading several groups of people including research nurses who are responsible for study accrual.*

Task 3: Get approval for the pilot study from all protocol review and human subjects review boards required and to set up the systems necessary to implement the study. *Task 3 is currently in progress and this was to occur over months 3-6. The questionnaire, data collection forms, local protocol review and local human subjects review approval has all been obtained and is ready. There has, however, been an extensive delay in DOD human subjects approval. There was a 7 month delay in receiving my initial MFR as the protocols related to the war with Iraq took precedence. Therefore, the human subjects review process is ongoing and the pilot study has not been activated and accrual has not begun.*

Tasks 4-7: Involve study accrual, data entry, analysis, report writing and strategizing the larger, definitive study. *Not yet begun due to DOD human subjects approval not yet obtained.*

Key Accomplishments:

- Publication of a research review article on libido published in the National Oncology Nursing Society Journal entitled *The Oncology of Nursing Forum* with the following reference Barton D, Wilwerding M, Carpenter L, Loprinzi C. Libido, as part of sexuality in female cancer survivors (2004). *Oncology Nursing Forum*, 31(3): 599-607.

- Pilot study, "Changes in ovarian stromal function in premenopausal women receiving chemotherapy for breast cancer" developed with team and receipt of Cancer Center and local Mayo Foundation IRB approval.
- This trainee gave a presentation at the nurse/CRA symposium for the North Central Cancer Treatment Group in April 2004, regarding endocrine changes in breast cancer survivors. Nurses and Clinical Research Associates from over 30 institutions across the US and Canada attended. This talk was a direct result of the ongoing literature review done to develop the pilot study associated with this grant as well as mentoring by endocrinologist colleagues on my research team.

Reportable Outcomes:

1. My mentoring and education task (task 2) has afforded me leadership involvement in working with three teams of research personnel related to symptom management, in addition to the team related to the pilot study on ovarian stromal function.
 - a. The first team is looking at the problem of fatigue and brainstorming research initiatives towards this end. This team consists of a psychiatrist, a biostatistician, a medical oncology fellow, and my mentor.
 - b. The second team is related to developing research looking at delayed nausea and vomiting. This team consists of a research nurse, myself, a medical oncologist, a biostatistician, and my mentor.
 - c. Finally, a brainstorming team was convened with significant leadership from myself, regarding hot flash research directions. This team involved an outside consultant, Dr. Robert Freedman from Wayne State University, a psychiatrist, a research nurse, medical oncologist, and my mentor. Ideas for future research and a comprehensive program to study these symptoms are being developed.
2. Regarding mentorship, I have been a part of two study sections for the National Cancer Institute/National Center for Complementary Medicine to improve my grant writing knowledge and skills.
3. In addition, I have done manuscript reviews for the journals, *European Journal of Cancer* and *Breast Cancer Research and Treatment* to sharpen my critical writing skills to improve my publication record.
4. Through my mentoring relationship, I have had a leadership role in the cancer control/symptom management program of the North Central Cancer Treatment Group. I have been involved in leadership meetings regarding budget management for two multi-million dollar grants as well as strategic planning for the symptom management program. I also serve as a resource to nurses throughout the United States who are members of NCCTG regarding implementation of symptom management clinical trials in their institutions. As a clinical researcher, being a resource to community sites gives me a particular insight into implementation issues in cancer centers with regard to clinical trials and will assist in future development and design of clinical trials that will be more easily implementable in community settings and more helpful to patients and families dealing with breast cancer diagnosis and treatment.

Conclusions:

Through the mentorship meetings and educational/brainstorming meetings that have occurred surrounding breast cancer symptom management, many opportunities have emerged that are allowing this trainee to have significant leadership roles in building programs of research and leading teams of people including nurses involved in accruing patients to clinical trials. In addition, continued review of the literature surrounding ovarian function and hormonal changes in breast cancer survivors as well as continued relationships with endocrine colleagues have resulted in increased expertise in this area and has led to a published review article in a peer-reviewed journal.

Finally, the pilot study developed under this grant, "Changes in ovarian stromal function in premenopausal women receiving chemotherapy for breast cancer" will potentially directly feed into the symptom management programs of fatigue, hot flashes and libido, all of which are clinical symptom management programs within a large oncology cooperative group (North Central Cancer Treatment Group). The potential for several RO1 funded grants exist as a result of this pilot work.

Statement of Work

Task 1: Work with a collaborative team to develop protocol of pilot study "Changes in ovarian stromal function in premenopausal women receiving chemotherapy for breast cancer", months 1 and 2:

- a. Meet with co-investigators to discuss salient issues for pilot study.
- b. Meet with statistical team regarding analysis plans.
- c. Draft protocol and send out for edits/input.
- d. Finalize protocol for submission to Protocol Review Committee.
- e. Based on the meetings with the team and endocrinologist consultant, one lab study was added to the project – an FSH was recommended to be obtained 3 times throughout the study to help in evaluating menopause status. Women were already being asked to keep a menstrual diary for this purpose. The FSH is a more objective, scientific measure to attempt to evaluate this. The other change in the study is that a bioavailable testosterone level will be drawn instead of free testosterone. This is because bioavailable testosterone takes into account the testosterone bound to albumin, which is a weak bond, and it is thought that this albumin bound testosterone is also physiologically available to the body and therefore, bioavailable testosterone is considered a more accurate measure.

Task 2: Attend mentoring sessions and educational meetings, months 2 through 24:

- a. Twice weekly meetings with Dr. Loprinzi.
- b. Weekly oncology core curriculum conference, breast committee and grand rounds attendance.
- c. Monthly cancer control meeting and monthly budget administration meeting.

Task 3: Get approval for pilot study, set up systems to implement study, months 3 – 6:

- a. Get protocol approved through Cancer Center Protocol Review Committee
- b. Obtain Institutional Review Board approval.
- c. Set up blood draws – research payment process
- d. Develop and copy questionnaire booklets
- e. Develop eligibility checklist and necessary data forms.

Task 4: Accrue to study, months 7 – 18:

- a. Work with nurse practitioners in breast clinic to identify eligible patients
- b. Educate, consent, follow patients through study

Task 5: Data entry and analysis, months 19-24:

- a. Set up data entry program
- b. Enter hematologic data and questionnaires
- c. Data cleaning and set up
- d. Preliminary analysis – look for problems, inconsistencies

Task 6: Final analysis and report writing, month 24:

- a. Complete final data analysis

- b. Write draft of results for publication
- c. Input for co-authors, team of collaborators
- d. Finalize article for publication

Task 7: Strategize follow up study and program of research based on pilot data, month 24:

- a. Work out details of needed follow up study based on pilot results
- b. Enumerate series of clinical studies to follow based on prior study
- c. Choose funding mechanism for immediate follow up study.